



1/30

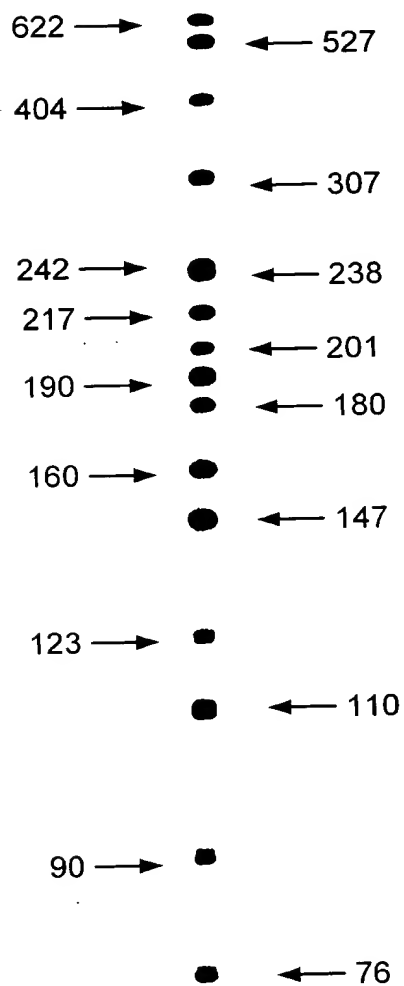


DIAGRAM 1

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FIG. 1A

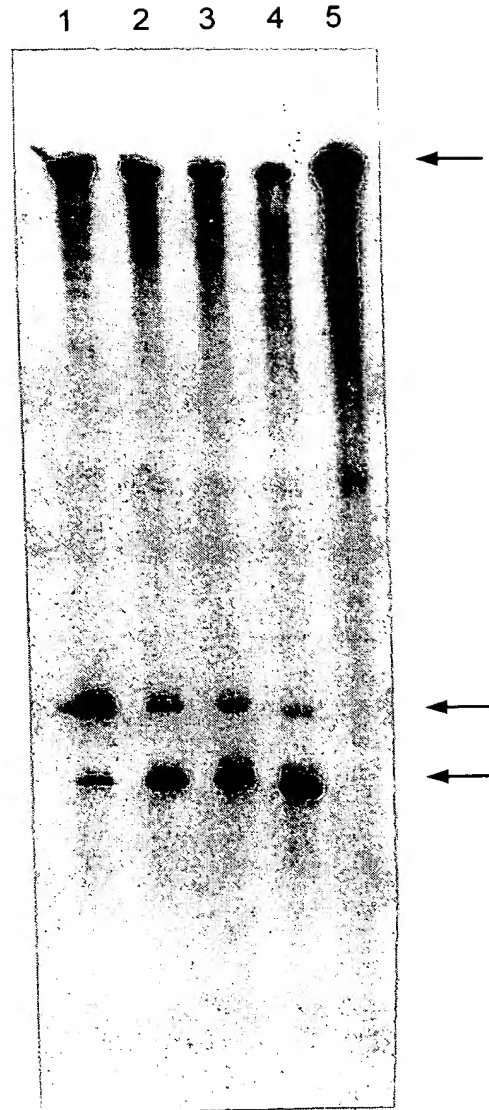


FIG. 1B

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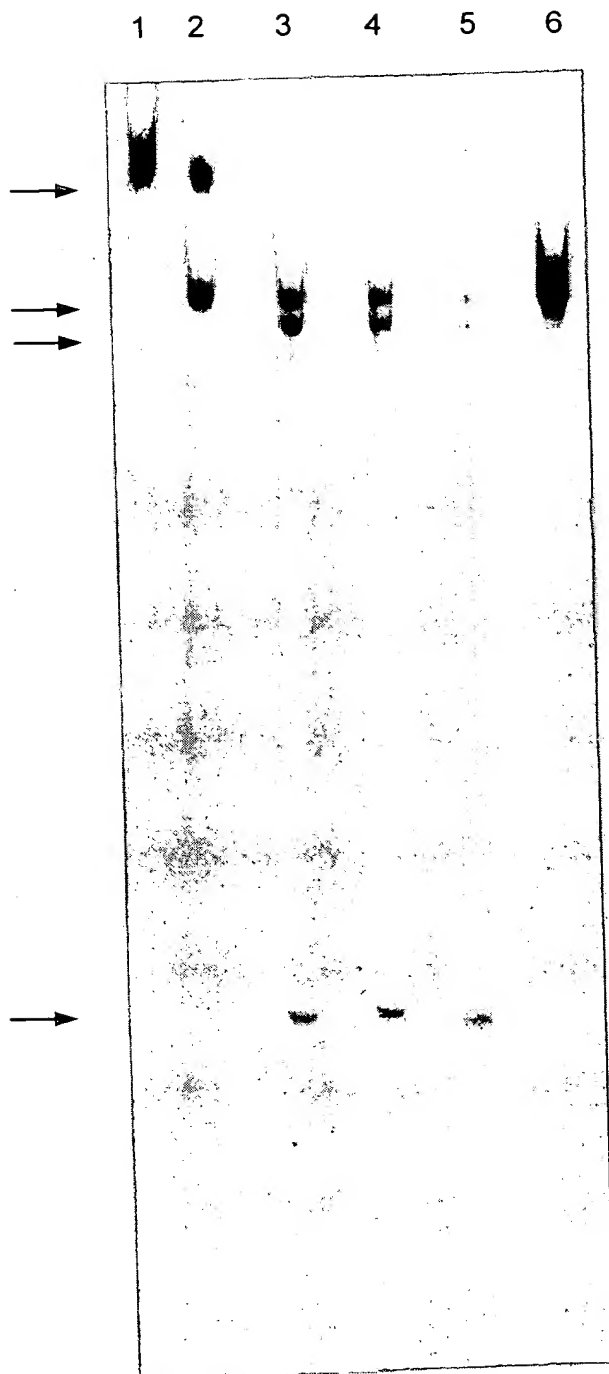


FIG. 2A

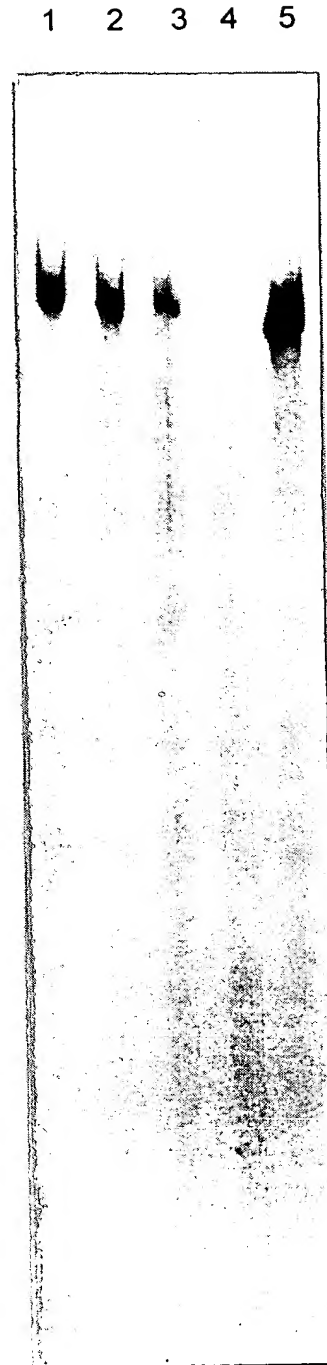


FIG. 2B

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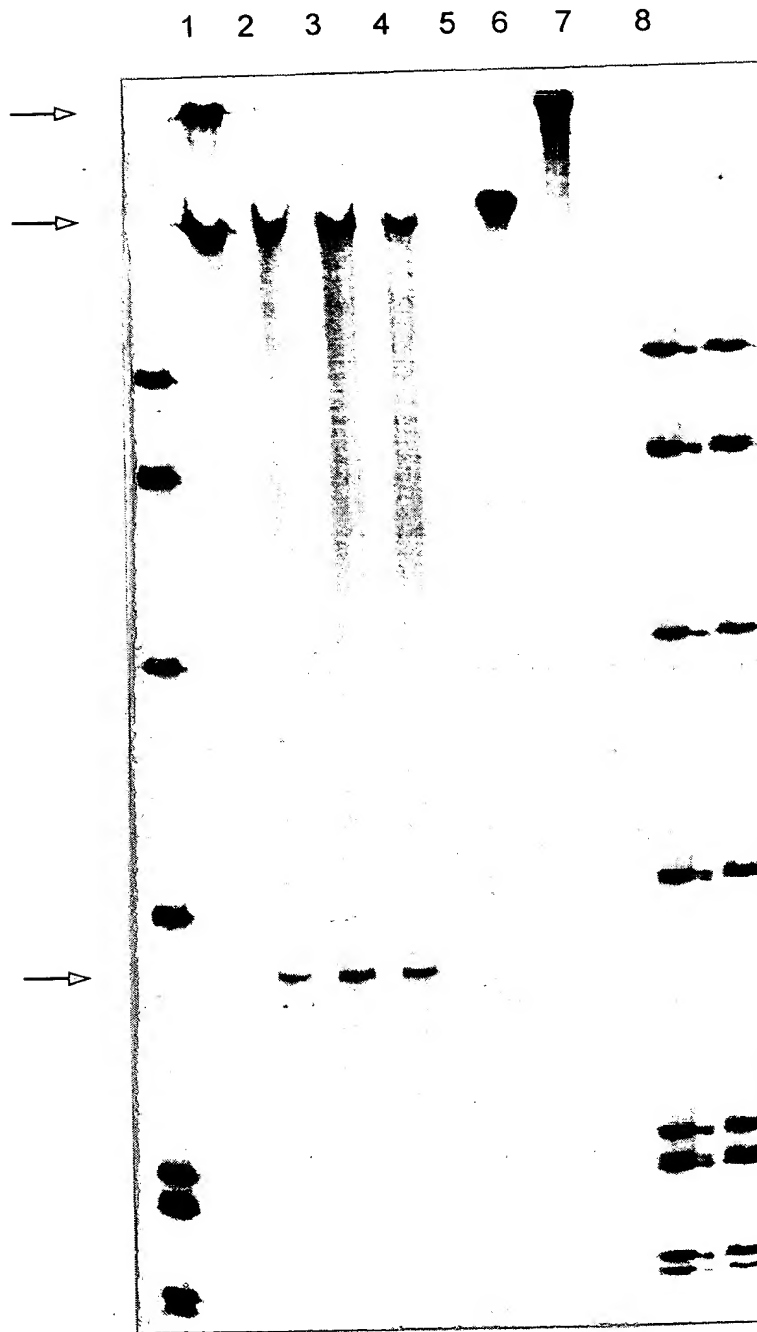


FIG. 2C

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1 2 3 4 5 6 7 8

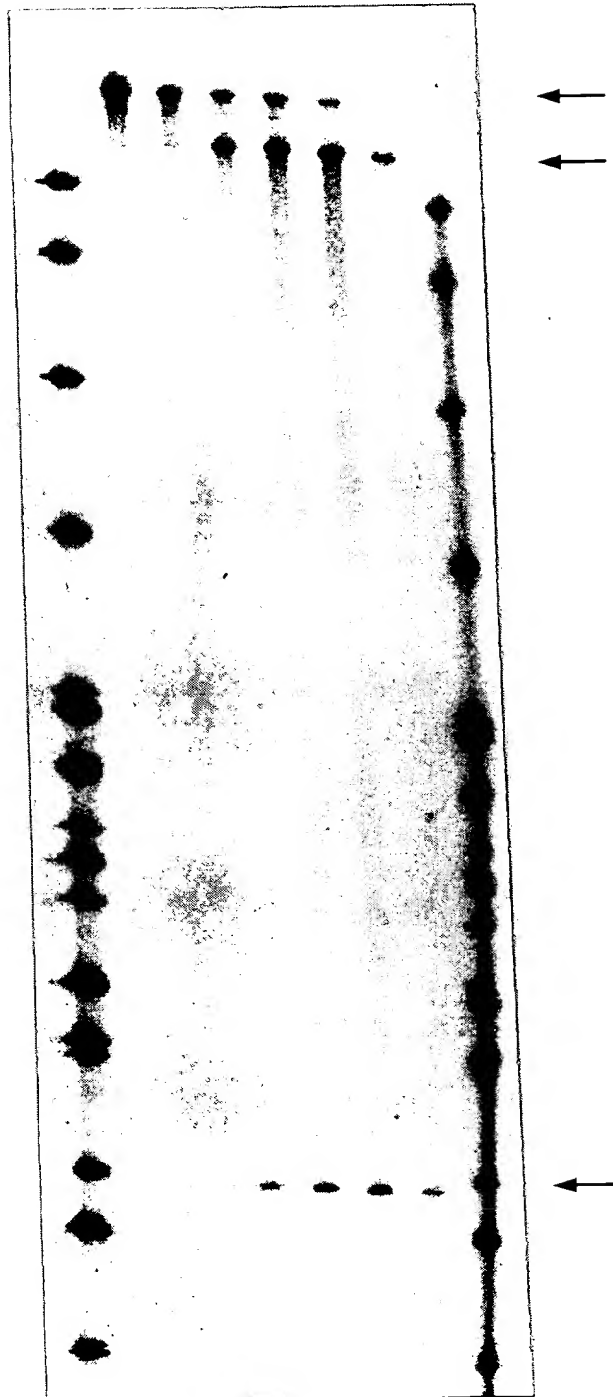


FIG. 3

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1 2 3 4 5 6 7 8

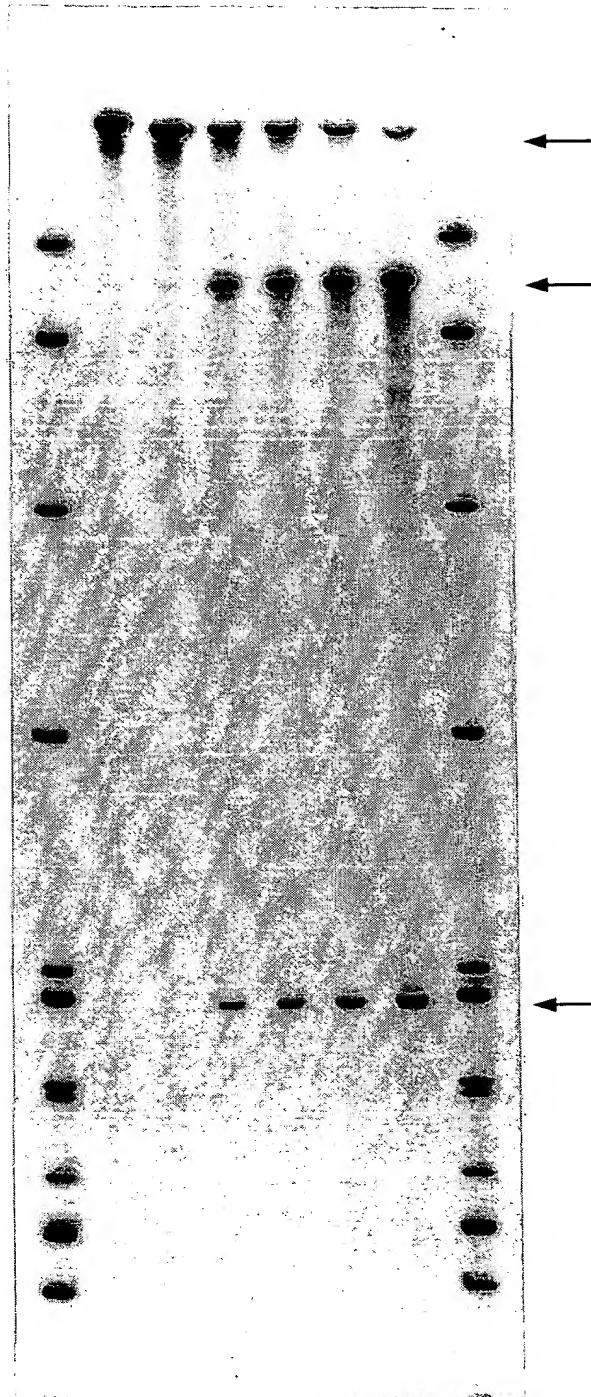


FIG. 4

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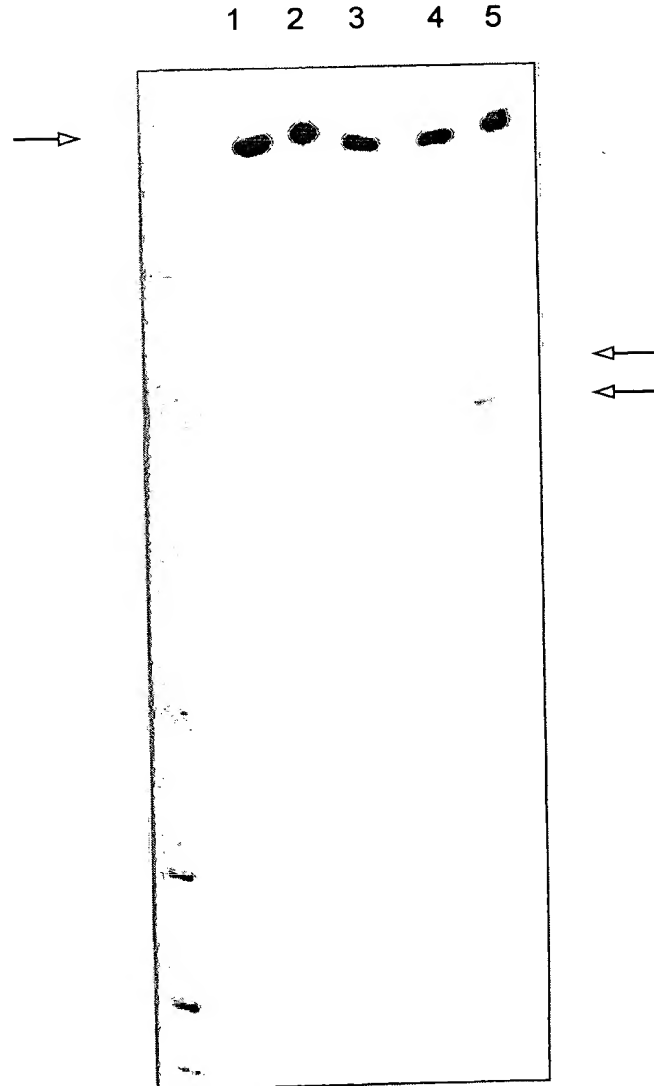


FIG. 5A

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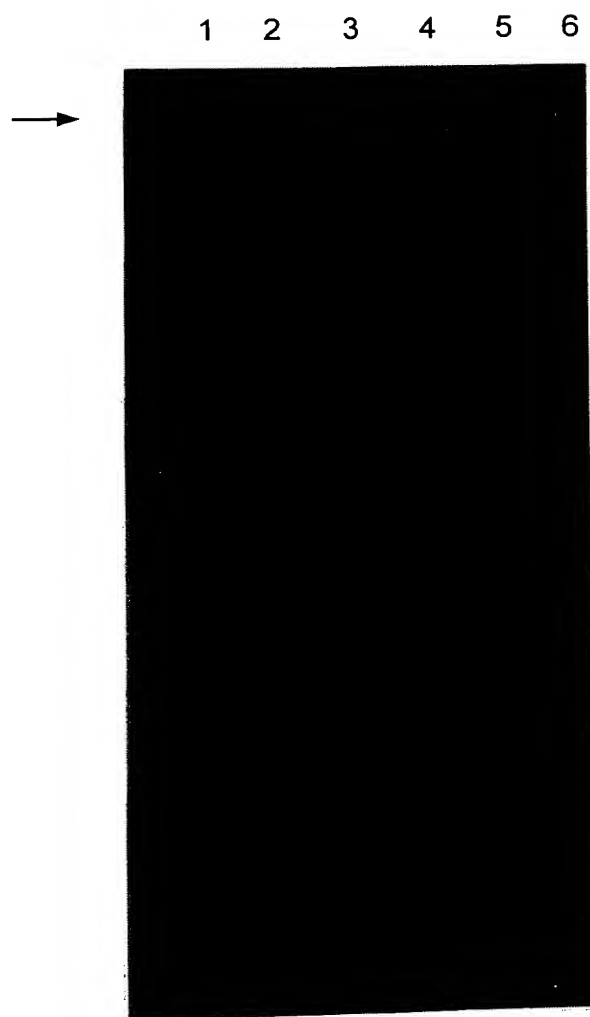


FIG. 5B

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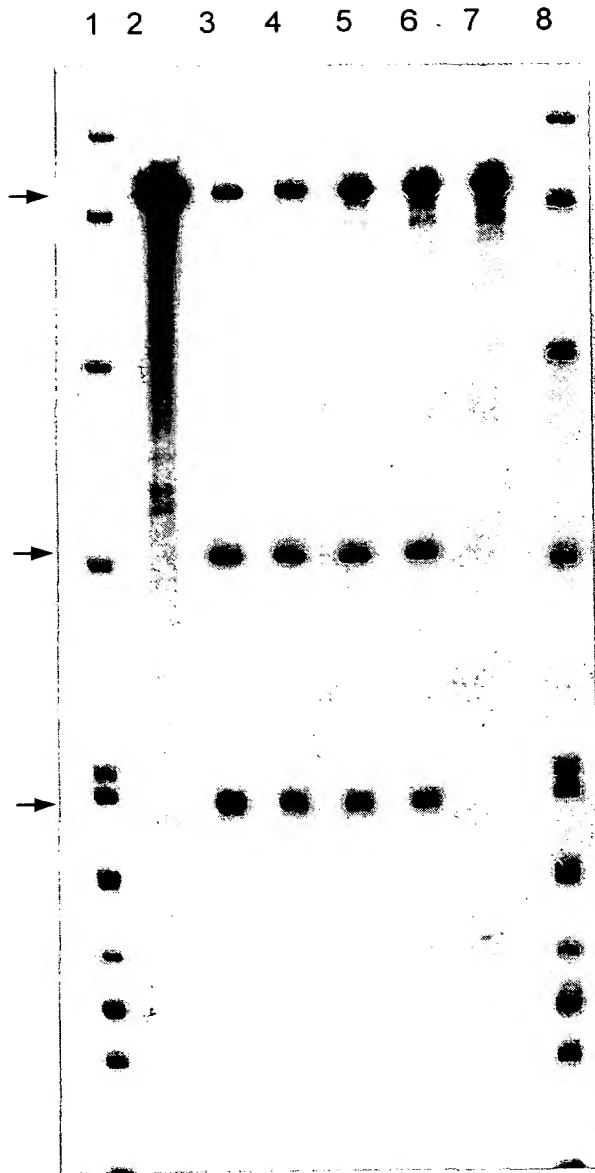


FIG. 6A

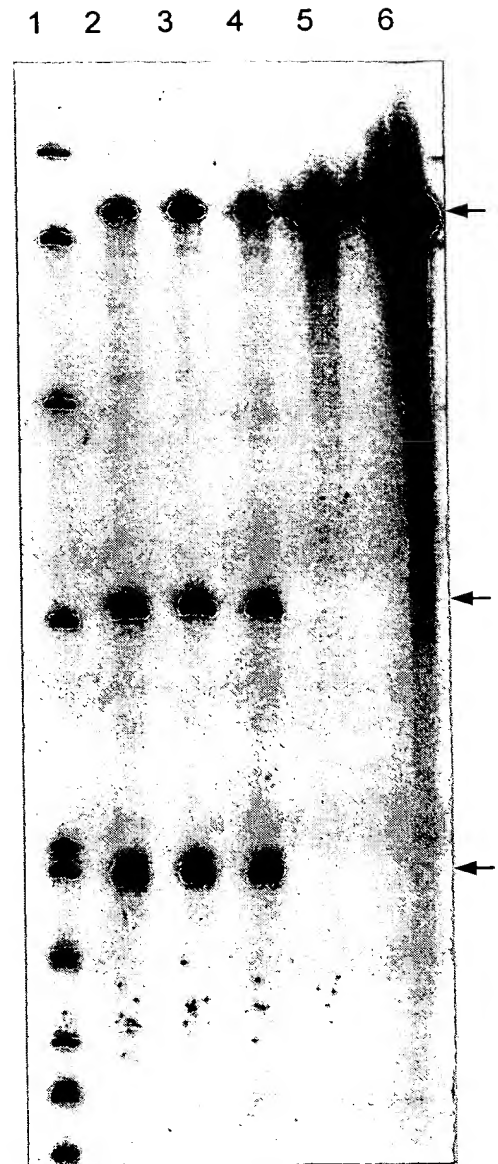


FIG. 6B

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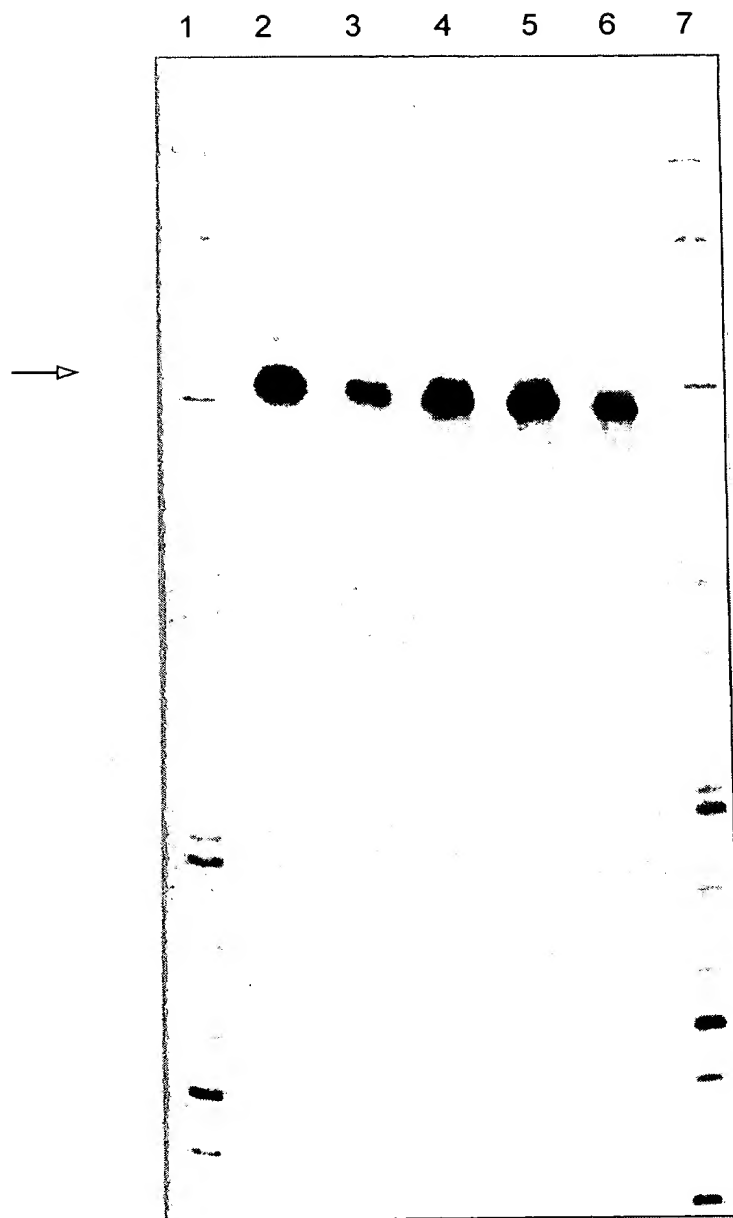


FIG. 6C

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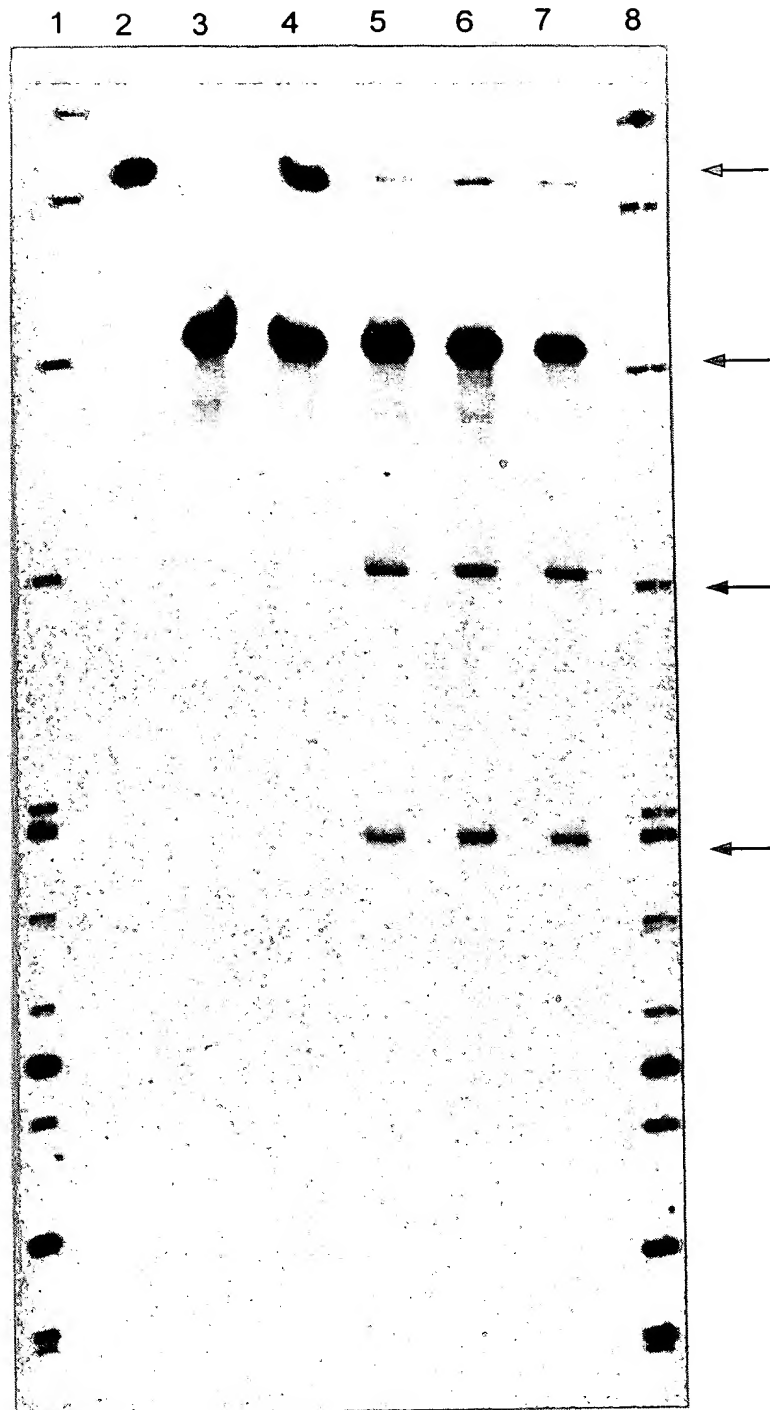


FIG. 6D

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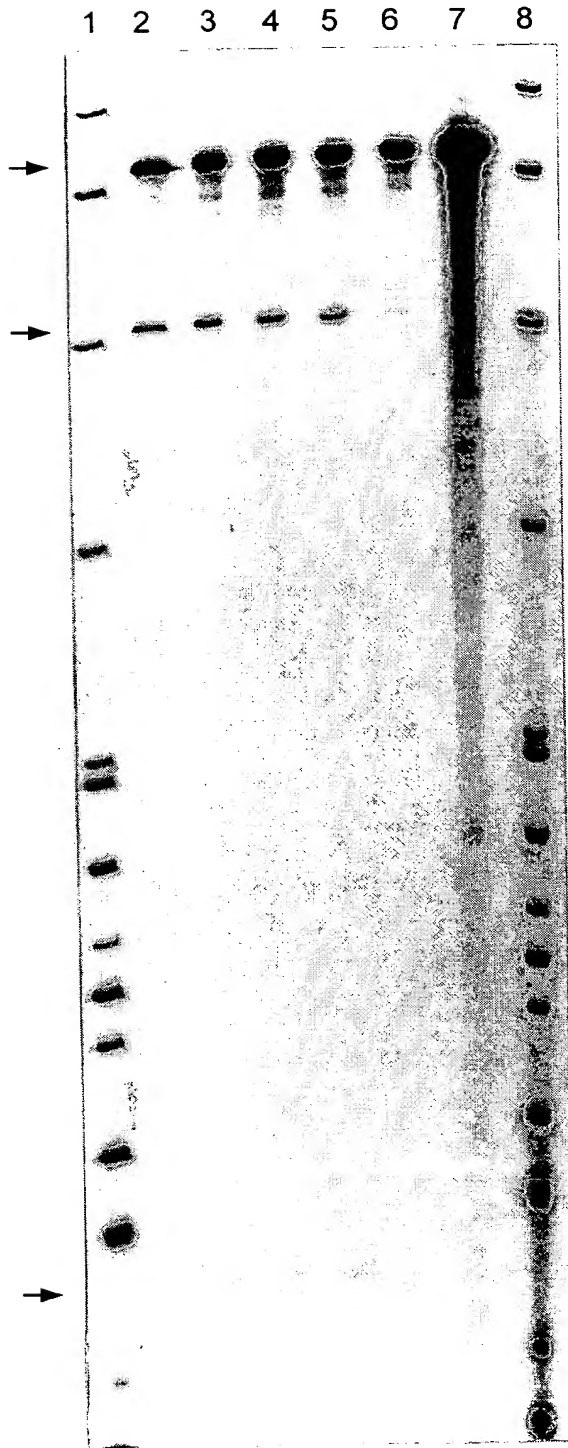


FIG. 7A

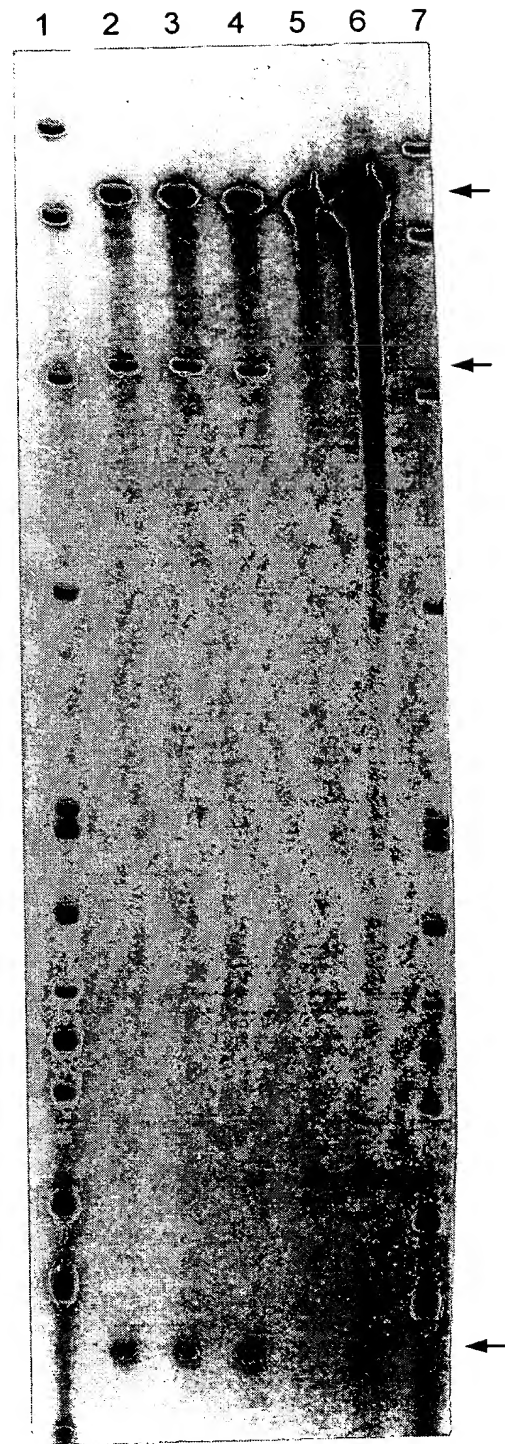


FIG. 7B

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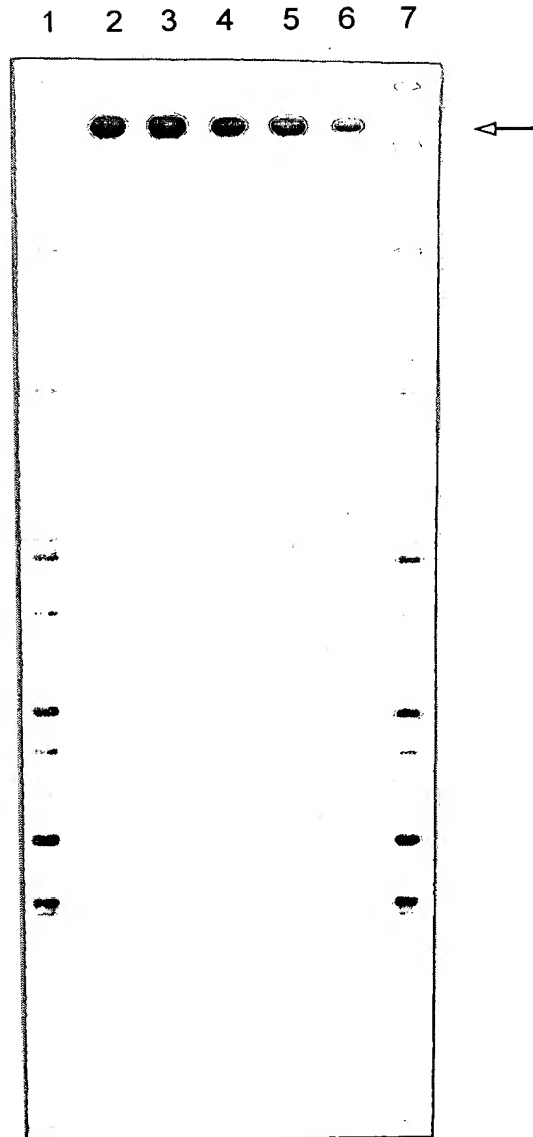


FIG. 7C

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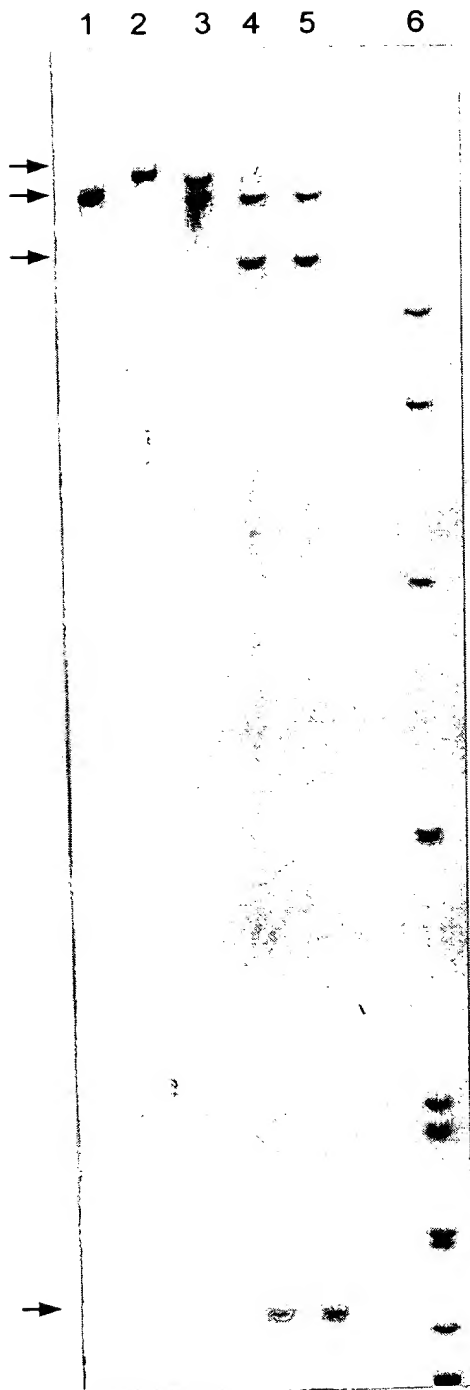


FIG. 8A

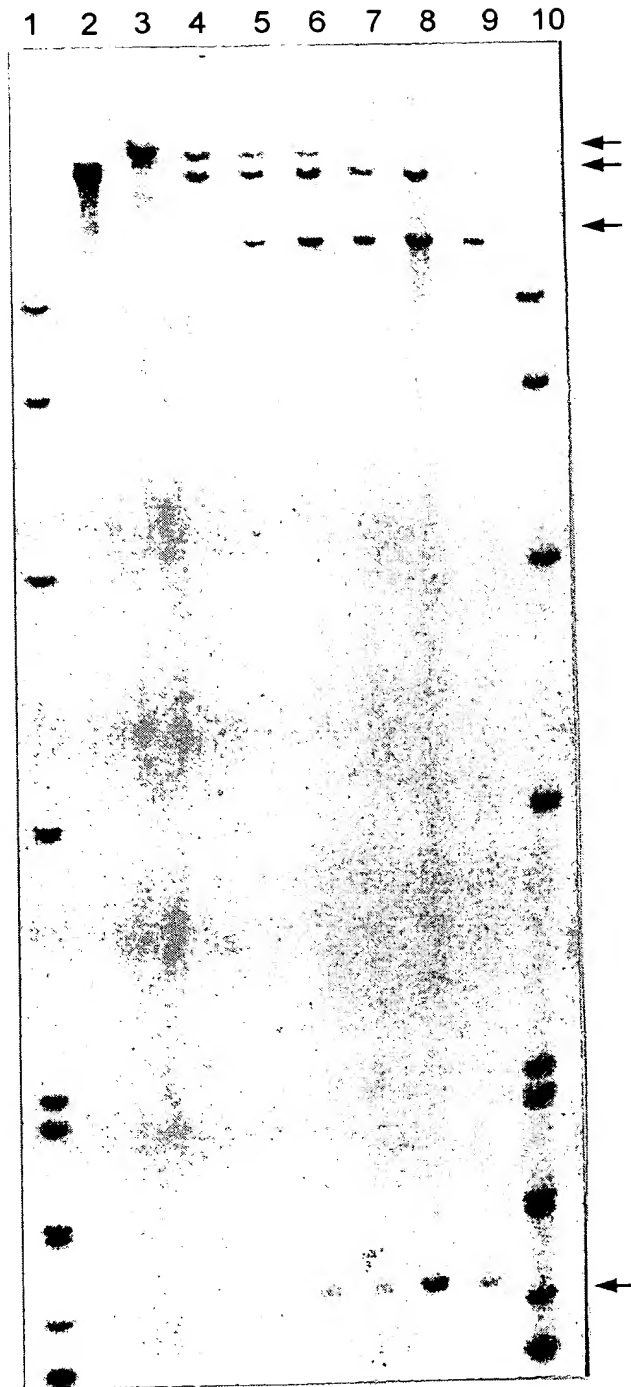


FIG. 8B

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Seq1 Human Rhodopsin

TCCCTTNTGNTAGATTGCANNNNCCCAATAAANAAGNCCCGCTTAAAGGCTTATCGAAA
TTAATACGACTCACTATANGGAGACCCAAAGCTTAGAGTCATCCAGCTGGAGCCCTGAGTG
GCTGAGCTCAGGCCTTCGCAGCATTTCTTGGGTGGGAGCAGCCACGGGTCAAGCCACAAGGG
CCACAGCCATGAATGGCACAGAGGCCCTAACTTCTACGTGCCCTTCTCCAATGCGACGG
GTGTGGTACGCAGCCCCCTTCGAGTACCCACAGTACTACCTGGCTGAGCCATGGCAGTTCT
CCATGCTGGCCGCTACATGTTTCTGCTGATCGTGTGGGCTTCCCCATCAACTTCCCTCA
CGCTCTACGTCAACCGTCCAGCACAAAGAAGCTGCGCACGCCCTCTCAACTACATCCTGGCTC
AACCTAGCCGCTGGCTGAACTCTTCATGGTCCCTANGTGGCTTCACCAAGCACCTCTACANCT
CTCTGCATGGATACTCGTCTTCGGGCCCCACAGGATGCAATTGGANGGCTCTTTGCACCTG
GNGGGAAATTGCCCTGTGGTCCCTNGTGGTCNGGNCACCAACGTAAGTGGTGTNTANCCC
AGAACAACTCCGCTCCC

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seq2 mut447

GGNNNTTGGTCGCGCATTAAGAACTCANGNCCCGCAGCAATCTTGGTGGGAGCAGCTACGGGTACGCCACAAGGG
CCACAGCCATGAATGGCACAGAAAGCCCTAACTTCTACGTGCCCTTCTCCAATGCCACGGGTGTGGTACGCAGCCCCCTTC
GAGTACCCACAGTACTACCTGGCTGAGCCATGGCAGTTCTCCATGCTGGCCGCTACATGTTTCTGCTGATCGTGTGGG
CTTCCCCATCAACTTCCTCACGCTCTACGTGACCGTCCAGCACAAAGAGCTGCGCACGCTCTCAACTACATCCTGCTCA
ACCTANCCGTGGNTGAACCTTTCATGGTCCCTAGGTGGCTTCAACCAACCTCTANACCTCTCTGCATGGANACTTCNTC
TTCCGGCCCCACAGGATGCAATTGGAAGGNTTCCTTTAACACCCGGGGGGGAAATTCCTGTGGTCCCTGTGGTCCG
GNCANCAACGGTACTTGTGGTNTTAANCCATAAACAAATTCGGCTTCGGGAAAAACATGCCANCNTGGGGTTTCCCTCA
CTNGGTTANGGCGGCTGCCCCCACCCCAATCCCNCGGTNGTCAANTAAATCCCAAGGCNNNANTGNCNTTTTAAACAAAA
AANNCCCCANTTGAGGNGNAAAAATTTTTTTTNNCCAANTTTNNNNNNNNNNNTTTTGNNGCTTCCCNCCNANNA
AAATNTTTNNTTTNGNNCCCTCCCCCNCNGAGGCGCCCCCNGATTNCCCAAAAGGAAAAAGGCCCCGGGCCCTNCN
TTNGGGGGGGCCCNNTNTTTTTTTTCCCCNCGGGGTNNCCNTTAAAAANNNTTTTNAAAACCCNTNNCTTTTTTTAA
AAAAACNNANCCCCCCCCNNGGNAAGGC

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seq3 Pro23Leu

NNNTTAGGNCGGATGTCNATATAAGCAGANCTCTCTGGGCTAACTAANAAGAACCCACTGGCTTACTGGCTTATCGAAA
TTAATAAGACTCACTATAGGGAGACCCCAAGCTTCCGGAAAGCCTGAGCTCAGCCACAAGGGCCACAGCCATGAATGGCAC
AGAAAGCCCTAACTTCTACGTGCCCTTCTCCAATGCGACGGGTGTGTACGAGCCTCTTCGAGTACCCACAGTACTACC
TGGCTGAGCCATGGCAGTTCTCCATGTGCGCCCTACATGTTCTGTGCTGATCGTGTGGCTTCCCCATCAACTTCCTC
ACGCTACGTACCGTCCAGCACAAAGAGCTGCGCACGCCCTCTCAACTACATCCTGCTCAACCTANCCGTGGCTGAACT
CTTCATGGTCCCTANGTGGCTTCACCANACCCCTCTACACCTCTCTGCATGGATACTTCGTCTCCGGGCCACAGGATGCA
ATTTGGAAGGCTTCTTTGCANCTGGNCGGAAATTGCCGTGTNGTCCCTGGTGGTCCCTGGCCATCAACNGTACTGTTGT
NTNTTACCCATNAACAAATCCGCTCCGGGAAACATGCACATGGGNTTGCCTCACTNGGTCGGGCGGCGNCCGCCACCC
CACCCCGGTGTCANTTATCCCANGGCGNAATGCCCTTNANNAAATAACCCACCGAGGTANAAATTTNTTTTATTT
TTGCCCNCCNCCAAANATTTTNTNGGGGGCCCCCNNAANNTTTNNNGNNNNCCNGGGGGGCGNCCCGNTTC
CCNAAGGAAAGNCCCGNCCCGCCNTCCNTTGNCCNCTGTAAATTNCCNGGGGTGNTTNTNAAANNTTTTANAAAC
CCNCCCTTTTNNNAAAAAANCNNNCNCCCCCNNNNAANNGAANNTCTCTTAAAAAANTCGCCAAANANTTTNANTT
NCCCCCCCCCCCCCN

CNCGNCGTTGAAATATAAGCAGACCCCTCTGGNTAACTANAATAACCACTGCTTACTGGCTTATCGAAATTAATACGACTC
ACTATANGGAGACCAAGCTTGGTCGGTCTGATGAGTCCGTGAGGACGAAACGTANANTCTANAGGGCCCTATTCTATAGT
GTCACCTAAATGCTAGANCTCGCTGATCAGCCTCGACTGTGCCCTTCTAGTTGCCAGCCATCTGTTGTTGCCCCCTCCCC
GTGCCCTTCCTTGANCTTGAAGGTGCCACTCCCAGTCTTCCCTAATAAAATGAGNAATTGCNTCTCATTTGCTGAGT
AGTGTCAATCCAAATCTGGGGGTGGTGGGCAGNACACNAGGGGAAGATGGAAACATACAGGCATGCTGGGGANGCCGT
GGNTCTATGNCTCNAGGGCGAAAACACTGGGGNCTAGGGGTACCCCAACCCCTGTACGGCCATAACNCNGNGGTTGTG
GTACCCACTAACGTANNTGCACCCTACCCGNCCTTCNTTCTCCTCTTNCCATTCCCGGTTCCCTCACCNAAACGGGCGCTTNG
TCATATCTNGGNCCACCAATANAGTAGTCTTTGCCCCCAAAGTCCCTNATGACCTNTAAGACCTTCANNANCCCCCCTT
NTTTNAAANANCCNNNNNNNNNNNNNNNNCCNGNAAAAANAACAACATAATTTGGGAACCCCCCCCCCNANAACCCCTTTCC
NTNTTCCCCCNATTAAATNTNNNTNCCCCCCCCCCCCCNNTTTTNNCNCNNNNNANNNGNNGNNCCCCCNNTT
TNAAAAAANNNAANNNCCCCGNNNNNAANCCCCC

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Seq5

CNCCCCGCCNNTTNAANAANCCNAGCCTCTGGCNAACCTANANAACCACTGCTTACTGGCTTATCNAAATTAATACGAC
TCACTATAGGGAGACCAAGCTTTACTCGAACTGATGAGTCCGTGAGGACGAAANGCTGCTCTANANGGCCCTATTCTAT
ANTGTACCTAAATGCTAGAGCTCGCTGATCAGCCTCGACTGTGCCCTTCTAATTGCCAGCCATCTGTGTTGCCCCCTCC
CCCGTGCCCTTCCTTGACCCCTGGAAGGTGCCACTCCCACCTGTCCCTTCTAATAAATGAAGATNTTNCATCNCATTGTCT
GAGTAAGTGTCAATCTATCTGGGGGTGGGTGGGCACGACANCAANGGGAAGATTGGGAAAAAATANCAGGCNTGC
TGGGATNCCGTGGGCTCTATNGCTTCTGAAGCGGAAAAACAACACTGGGCTCTANGGGTATCCCCCCCCCTGTAAAC
GNGCATTAAACNCGGGGTGTGTGGTTACCCCAACTTAACGCTANCTTGCAACGCCCCNAACGCCCCNCCTTTCCTTCT
CCCTTCCTTCNCCCACTTTCGGGTTCCTCCNTCAACCCNAATCGGGGCCCTTAGGTCCAATTATGCTTCGGCCCCNCCCN
AACTAATAGTNGGTTCTTTNGCCCCCCNAAAAANTTNCCCCNATTGATCCTCCNNAANAACCTTCCCCGAAAAANA
CCCCCCTCANNNCNTCTNCAANNANNNCCCCCNCNTTTTATAAGGATNCAACCCCTTTTAAANANAAAAATACAAAT
CTTNTTTTGTGGTTNCCCCCCCCCAAAATNCCCCCTTCTCCCTTTTCCCCCCCCCAATAACTCTNTTTNCNATNCC
CCCCCCCCCNCNCNTCNCNNNNNNNTCTTTTNTTNCCTCCCTCCCNATNNTTTTTCCTCCNCCTCCCCCCCCC

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Seq 6 mouse rhodopsin

TCAGTGCCCTGGAGTTGCGCTGTGGGAGCCGTCAGTGGCTGAGCTCGCCAAAGCAGCCTTGGTCTCTGTCTACGAA

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seq7 m rho mut 1460

NNNTCTCCNCTTTCGTTTGTGNANANTCANNAAANANAGCGNCCCGGAAGGTGTCAGTGCCCTGGAGTTGCCGCTGTG
GGACCCGTCANTGGCTGAGCTCGCCAAAGCAGCCTTGGTCTCTGTCTACGAAGAGCCCGTGGGCGAGCCTCGAGAGCCGCA
GCCATGAACGGCACAGAGGGCCCCAATTCTATGTGCCCTTCTCCAACGTACAGGCGTGGTGGGAGCCCTTCGANCN
TCCGCACTACTACCTGGCGGAACCATGGCAGTTCTCCATGCTGGCAGCGTACATGTTCTCTGCTCATCGTGTGGGCTTCC
CCATCAACTTCCTACGCTCTACGTACCCGTACAGCACAAAGAGTGGGCACACCCCTCAACTACATCCTGGCTCAACT
TGGCCGNTGGGNTTGGAACTCCTTCCCATTTGGGTCNTTCCCGAANGGANTNACCAACCCCTCTAACACATCAA
CTCCCATGGGCTACTTCGTTCTTTTGGGCCCCNAGGCTGTTAATCTCGAAGGCTTCTTTGCCACACCTTGGAAAGTGAA
ATCNCCTGTGGTCCCTGGTGGTCNTGGCCATTAAAGCTACTTGTGGTCCCTGCAACCCCAATAACAATTCCGCTTCCGGG
GAAAANNACCCNCCATGGGTTTGGTCNTCCCNNGANTTAAGGTTNGGNTNNNNGGCCCCCNCCCCCTTGGGNNGTC
CANNTNATTNCCCGANGGNGCCATT

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seq8 RIB33

TCCCCCTNNNTTTTGTAGCNCTGCCAANAAAAAGGCCAGCTCACAGGANAANTANANAACCCACTGCTTACTGGCTTANC
NAAATTAAATACGACTCACTATAGGGAGACCCCAAGCTTGGCACATCTGATGAGTCCGTGAGGACGAAAAAATTGGTCTACA
GGCCCCATTCTATAATGTCACCTAAATGCTANAGCTCGCTGATCATCCTCNACTGTGCCTTCTACTTGCCAGCCNTCTN
TTGTTTGGCCCCCTCCCCCGTGCCCTTCCTTGACCCCTGGAAGGTGCCACTCCCCACTGTCCTTCCCTAATAAATGAGGAAATT
GCATCGCATTGTCTGAGTAAGTGTCAATCTATTCTGGGGGGTGGGGTGGGCAGGACNNCAAGGGGAAGATTGGGAAAT
ACAATANCCAAGGANCNCTCCCCCNCGGTAATTGCGGATTNGGCTCTNTCGCTTCCCTAAGGCNGAANAACAACACTNGG
GCGCTNCGGGTTTCCCCCNCCNCCCTNTTAGCNGCGCATTANTCGCCGCGGGTGTGTGTACTCCCCACCTNAACG
CTACANTTGCCAGCGCCTAACGCCCCCCCCCTTNCNTTCTTCCCTCCTTCTCNCACCTTCCCCGGCTTCCCCCNCCANCC
NAAATCNGGGGNCNNAGGTCNCAATTANTGCTTANGCCCCCCCCCACTTAATTNNGTTNTGTTCTCTTTTA

seq9 HUM RDS

[illegible]

seq 10 h per mut 257

[illegible]

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seq11 h per mut (359)

TTTTNTGGNTNTCNAATTAAACGACTCACTATAGGGAGACCCAAAGCTTGGTACCGAGCTCGGATCCACTAGTAACGGC
CGCCAGTGTCTGGAATTCTTCANCGCCAGGACCCAGGACTATCCCCCTGCTCAAGCTGTGATTCGAGACCCCTGCCACC
ACTACTGCATTACCGGGATCCAGGCTAGTGGACTCGACATGGTAGCCCCAGGGCAGCTCCCTACAGCTTGGGCCA
TCTGCACTTTTCCCAAGGCCCTAAGTCTCCGCCCTCTGGGCTCGTTAAGTTTGGGTGGGAGCTGTGCTGTGGGAAGCAA
CCGGACTACACTTGGCAAGCATGGCGCTACTGAAAGTCAAGTTTGACCAAGAAAANCGGTCAAGTTGGGCCCAAGGGC
TCTGGGCTCNATGNAAACCTNGGTTTCCCCCCCCCTNTTTGGGCTGGGCATCATCTTTAGCCCTGGGANTGTTCCCTG
AANATTGAACTCCCAAGAGANCGATGTGATGAATAATTCTGAAANCCATTTTGTGCCCCACTCATTGANAAGGANGGGG
TGNATCCTGTTTCTTCACTCCCTGNTGGAAAATGCTACAANCCCTGAACCAACCCATTTCCCAANGAACCNNGNTGAAA
CCNTACCNCGGTTTNTTTTCCCTNAAACANCCCTCCCCTTTGGCCCCCGCGNTTNCGCTNCGGGNCCCNAAAAACCNNGG

N

[illegible]

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seq13 rib31

NNTTNTCCTACGNCCTTTTAAANANAACCAGACCCCTCTGGANAATTANATNNCCACTGCTTACTGGCTTATCGAAATC
AATACGACTCACTATANGGAGACCCCAAGCTTACAGTCCCTGATGAGTCCGTGAGGACGAAAGGCTGAATCTANAGGGCCC
TATTCATAGTGTCACCTAAATGCTAGAGTCGCTGATCAGCCTCGACTGTGCCCTTCTAATTGCCAGCCATCTGTTGTTT
GCCCCCCCCGTCCTTGACCCCTGGAAGTGCCACTCCCACCTGCTCCTNTCCTAATAAAATGATGANNNTGCATCG
CATTGTCTGAGTAAGTGTCACTATTCTGGGGGTGGGTGGGCANGACANCAAGGGGAAGATTGGGAAAAACATTN
CACGCATGCCGGGGATGCGGTGGGTCTTNTTNGCNTCNGAAGCNGAAAAACNACTGGGGCCCTANGGGTNNCCCN
TCCCCNTGTAAACNGNCCTTNAACNCGGGGTTGTGGTTNNCCNANCTTANCNCTNAACTCCNNCCCCNNNCCCCCNC
TCTTCCCTTTTTCCTCCATCTCCNCNTTNNCCGNTCTCCCTTNCACNAATGGGGCCCCACNGGGNCTNTNTCT
CTTNNNNCCNCCNANANATATNCTNCTATCTNCTANAANCNCTCCTCGGCCCTCANNANCNNTTCTCTNCNCAANNCCNC
CANNNCACTCCCCCTTNCNTATCCCTNCTATCTNCTANAANCNCTCCTCANNCCCCNCTANATANCCNAANCCCTCN
CACCCCTTACACACNTCTTCCCCCTCTNNNNNCATCTCCTCTCTNCCNCCNCCNCTCCTCCCCCTCNNCTTCTACTCN
CTCANNNGTCTNCNNTCCCTCTNNTNNACTNCCCTCTCTCTCTNCCNCCNCCNCTCCTCCCCCTCNNACCCCTNNTCGNCATC
NTNNNTTCTNCCCTNCTACNTCCCCNTNTCCCCNTTCTCNCNNCTCTNCTCTNTNNCACTCACCCCTNCNGCTCNNCTC
TCTTCTCNCNTCTCCCCC

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seq14 PCR3 polcoll1a2

NTCNCGNCATTTAANCAGGCCAGGNCCTACCGCNCNGGTCCANGTAGGCCGGGAGCCCCAGCAACGCCGGGAAGGCCAGCAG
CACCCCTTGGCACCAAGTAAAGGCCGTTTGCTCCAGGATTACCANAGAGGTCCACGGGCCGGAGAGGCTGGAAANACCACTT
CACACGGGGAAACCGCGGGTCCAGTAGGACCAAGCGTTACCAACAGCTCCAATTTCAACCCTTGGGGCCAGGGGCACCTGG
GAAGCCTGGANGGCCAGCAGACCAATGGGACCAGCAGGACCAACGGACCACTTCCATCACTGCTTTNGCNCAGCTGGGC
AAGGCACAACACTTCTCTCACANGAACCCACGGCTCCTGTTTNACTGAATCCATTTACAGGGCACAGTTCACCTT
CACACAAGAACACGGNTGTCTTCATCATCAGACATGTTCCCTAATGCTTGAGCAGANTCAGATTCAGGAAACACACAC
CTTTGTCCACATCTCTNCACAGTCTCGGTTTCAGGTACACTCCCCACCTGCAGAGGCACCTGACCAACCTGAGACATTGACA
TTNCAGNCCACAGTCTGAAGTGAAGCGGGCACGCCATGGCNAAGTCATACCTGTCAAGNATCATCTTCTTANCAATCCCCAA
NGGGCAGAAATGAAAGCTGACTCCCCAATGTCTTATTTTAANNANGGTTTNAANAANNNNNNNNNNNNNNNNNNNNNNC
CCCCCCCCCTTNGGGTTTATTATCTATNCNCCCNCTNGGATATCTTNNCCCCCTTNAANTTTTNTTNTTTT
TNNNNNNNGGNTNNTTTTNNNNCCCNNTTTTNTTTTNNNGGGGNNTTT

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seq15 tot polcolla2

CCCTTTAAACANGGCCAGGAATACCGCGGGGTCCAGGGAGGCCGGACCCCANCAACGCCGGGAANGCCAGCAGCACC
CTTGGCACCAAGTAANGCCGTTTGCTCCAGGATTACCAGAGGTCCAAACGGGGCCGGAGANGCCTGGAAAGACCACTTCACC
ACGGGAACGGCGGACCAAGCANGACAGCGTTACCAACAGCTCCAAATTTCACCCCTTGGGGCCAGGGGCACCTGGGAAGC
CTGGANGGCCAGCAGACCAATGGGANCAAGCAGGACCACGGGACCACACTTCCATCNCCTGCCNCTGGCACCACTGGGCAA
GGCACAACACTTCTCTCACNAAGAACCCACGGNTCCTGTTAACTGAATTCCATTTCACAGGGCACAGTTCACCTTC
ANACAGAACACGGGTGTCCTTCATCATCAAAACATNTTCCCTATNCCCTTGAGCAGAAATCAGATTCAGGAACACACACTTTC
TCACATCTCCTCACAGTCTCGGTTTCAGGTAACACTCNCACCTGCAGAGGCACCTGACNAANCTCAGANATTANATTCN
CTCCNCAGTTTGAACTTAGCGGGCCCTNNCATTTGGNTTGTCCCTAACCTNTNGGGGTTTTCCTTNNNNNNNNNNTTT
NACNANTCCCAANGGGGANAANAGNTGACTCCTATGTCCTTNTNTNAAAAGGTTTTTNAAAAATTAACCCCCCCCCCTN
TTGGGTTATTATTTTTTTNNCCCCCTTTTNGAANCNTNNCCCCNTTTTCCCCNNNAAANTTTTTTNTTTTTTTGNN
NNNNTTGGGGTTNNTTTNTNNCCCCNNTTTTNANTTNGGGGT

30/30

seq16 RIB908

NCTTTCNNTCTNATNCAANAAGCAGGCCCTCTNNAAAACTANANTTCCACTGCTTACTGGCTTATCGAAANCAATAC
GACTCACTATAGGGAGACCCCAAGCTTCGGCGGCTGATGAGTCCGTGAGGACGAAACCAGCATCTAGAGGGCCCTATTCTA
TAGTGTCACCTAAATGCTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTGTTGCCCCCTC
CCCCGTGCCCTTCCTTGACCCCTGGAAGTGCCACTCCCACTGTCTTCTAATAAAATGANGAAATTCATCGCATTTGTC
TGAGTANGTGTCAATCTATCTGGGGGTGGGTGGGCANGACANCAAGGGGAAAGATTGGGAANACATAACAGGCAT
GCTGGGGATGCGGTGGGCTCTATGGCTTCTGAGGCGGAAAGAACCAACTGGGCTCTANGGGGTATCCCCACNCCCCTGT
TACCGGCGCATTAANC GCGGGGTGTTGTGTTACCCNCAACTTAACGCTACACTTGCCACGCCCTAACGCCCTCCTTTC
GCTTCTTCCTTCTCCCACTTCCCCGNTTTCCTTCAACTCTAATCGGGCNCCTTAGGTCCAATTAATCTTACGGN
CNCACCCAAAACCTNATAGGTAAGTCTTNTGGCCCCCCTAAAGTTCCCCCTAAATGAATCANNCTAAATGAACNTTCNA
GGAAACCCNCCNCTNCTTAAANGAANNNNNNCCCCNNNAAAAAANNNNNNNNNNNNNNNNNNNNNNNNN
NNNAAAAANCNNNATTTTNGGTGAACCCCCCGNAATTAANTCCNTTCNC'TTTTCCCCCNANNANNNNNTTNNN
NNNNNTCCNNCCNNNNNNNNNCCNNTTTTNNNNCCCCCNNAANANTTNGNNNNCCNNNNNTTTTAA
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